

August 27, 1956

Dear Jacques:

I am sorry to have taken so long to read your ms., but it arrived while I was away on vacation, and I have tended to it at my first opportunity. I have just forwarded it to Sol. Boris Rotman has returned to Chile—address below—and I will ask Sol to pass it on to him.

I don't have to tell you that this is an interesting and exciting story. There is just one experimental fact, however, that I feel is lacking for the understanding of the functional relationship of γ and *in vitro* galactosidase activity. When I ran into the discrepancy ~~mix~~ between intact-cell and extract activity, this notion was of course obvious and preminent, but I was puzzled by the failure of azide to influence the activity of the intact cells. And I still am. If the permease is sensitive to azide, and is necessary for *in vivo* activity, why is there no effect? Should not an azide-treated suspension of induced or constitutive cells behave like the induced or constitutive Lac^- ? It therefore seems to me possible that the γ -system does not influence the rate of transfer of substrate into ~~the~~ cells, despite its other remarkable properties. Or do you have a direct measure of this rate, which I have overlooked?

For my own clarification too, you have mentioned that Lac^- is a crypticity mutant. Do you happen to have any experimental figures comparable to that of Table 7 for the K-12 mutant? I might have missed the effect from using as controls cultures that already had a ~~mix~~ crypticity factor of about 100. Is it possible that Lac^- has a different pattern of change of crypticity on aging than does Lac^+ ?

On p. 18, you refer to the accumulation of UDPG, demonstrable in Lac_2^- and Lac_4^- , but you have deleted the experimental proof of it; I would hope that you would restore this missing table, as it is very difficult to make a critical appraisal of the discussion on functional relationships without it.

Kulchick and Kurcheski have been studying the galactose enzymes of our mutants. As you know, they recognize three enzymatic steps: 1) Gal + P — Gal-1-P (kinase); 2) Gal-1-P + UDPG — Glc-1-P + UDPGal (transferase); 3) UDPGal — UDPG (galactonase). So far, Gal₁; Gal₄; Gal₆ and Gal₇ mutants lack the transferase (as do the galactosemic mutants of *H. sapiens*); Gal₂ lacks the kinase. No galactonase mutants so far (they may be blocked in a vital synthesis of galactose; we should look for galactose-dependents!). These mutants are, of course, all very closely linked. But another Gal-, not linked to these, and not in the lambda-transduction region is also kinase-negative. These findings are all preliminary; we are looking for more electrons while K&K continue their analyses. (It is true that Gal_{1,4,6,7} belong to one position-effect group, but I hesitate to draw even the obvious conclusions until we have more data).

Thank you very much for letting me read your ms. With best wishes,

(C → Sol.)